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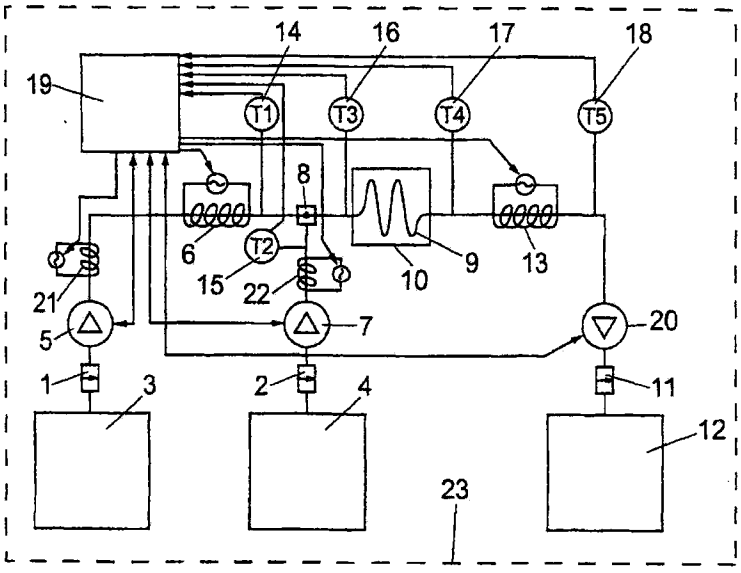


(57) Abstract: A method and a cycler intended for peritoneal dialysis, comprising a pressure chamber (201) provided with a first bag (202) for enclosing a fresh fluid intended to be filled to a patient and a second bag (203) for enclosing a spent fluid intended to be drained from a patient, said first and second bag being arranged at a weighing device (215) for weighing the combined weight thereof. A draining device is arranged for draining the spent fluid into the second bag supervised by the weighing device (215), and a replenishment device (204, 205, 206) is arranged for replenishing said first bag at a predetermined replenishment fluid flow rate during said draining step. Thus, time is saved and the peritoneal dialysis can be performed in a more efficient manner.

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TITLE

# METHOD AND CYCLER FOR PERITONEAL DIALYSIS

## FIELD OF INVENTION

The present invention relates to a method and cycler for the administration of a sterile medical fluid, such as a peritoneal dialysis fluid. More specifically, the invention relates to a method and device for operating a cycler for decreasing the cycle time.

## PRIOR ART

Medical fluids intended for mammals, specifically for use in humans, are required to be sterile before being infused or applied to the mammal.

One available method for sterilizing a fluid is to heat the fluid to a sterilizing temperature and to hold the fluid at the sterilizing temperature during a sterilizing time. To obtain a sterile medical fluid intended for infusion, the fluid is normally heated in an autoclave to 121°C for 20 minutes to thereby produce said sterile medical fluid. After the sterilizing time has elapsed, the fluid should be cooled to a physiologically acceptable temperature before infusion.

Known methods and apparatus for sterilizing a fluid are disclosed in for example GB 1450030, GB 1504334, GB 2034584 and US 5603894. These prior art publications describe the preparation of a medical fluid starting from tap water and producing pure water via a reverse osmosis device, mixing a concentrate with the pure water to produce a non-sterile medical fluid, passing the non-sterile medical fluid through an on-line autoclave and

delivering the sterile medical fluid to a recipient, such as a storage bag or a patient.

In the prior art, the complete medical fluid is first prepared in a non-sterile condition and then passes through an autoclave. If the medical fluid comprises heat sensitive components, these must not be exposed to too high a temperature. Normally, the temperature is increased up to the sterilizing temperature and the medical fluid is maintained at the sterilizing temperature for a sterilizing time. If the temperature is 121°C, which is normal in an autoclave, the sterilizing time is 20 minutes to obtain a sterilizing dose $F_0$ of 20 minutes, see below for further details. Since the sterilizing effect is approximately exponential, an increase of the temperature by 10°C means a lowering of the sterilizing time by ten times. If a sterilizing temperature of 131°C is used, the sterilizing time should be 2 minutes, and if a sterilizing temperature of 141°C is used, the sterilizing time should be 12 seconds, in order to obtain a sterilizing effect $F_0$ of 20 minutes.

The fluid thus produced should be provided to a patient. For peritoneal dialysis, normally a cycler is used for introducing and removing the fluid to and from the patient. One such cycler is disclosed in the publication WO 95/20985 assigned to applicant, the content of which is included in the present specification by reference.

The cycler according to said publication is provided with a pressure chamber enclosing two bags, a heater bag and a drain bag. The bags may be arranged as a double bag. The bags are arranged on a weighing device, such as a pair of scales. The weighing device controls the weight of the combined bags, and valves control the flow of fluid into and out of said bags in order to perform a patient drain and a patient fill. Moreover, the cycler replenishes the heater bag from a supply of fresh fluid and empties the drain bag to a waste receiver.

According to the present invention, the fresh fluid may be provided from an autoclave which is typically only operated at a constant flow rate which should be as low as possible for reducing the requirement of heat transfer during the autoclave cycle. Thus, the replenishment fluid flow rate is relatively low.

However, the efficiency of the peritoneal dialysis is dependent on inter alia the number of exchanges of fluid during a treatment period, such as a night. Thus, in some case, the said low replenishment fluid flow rate may be limiting for the efficiency of the treatment.

Thus, there is a need for a method of operating a cycler of the type mentioned above, in which the replenishment time may not be a hindrance for the efficient treatment. This is more important when the cycler is directly connected to an on-line autoclave, having a reduced replenishment fluid flow rate which moreover should be constant.

## DISCLOSURE OF THE INVENTION

Accordingly, a main object of the invention is to provide a method and a cycler in which the cycle time is reduced, in spite of a limited replenishment fluid flow rate.

Thus, there is provided a method of operating a cycler and a cycler intended for peritoneal dialysis, comprising a pressure chamber provided with a first bag for enclosing a fresh fluid intended to be filled to a patient and a second bag for enclosing a spent fluid to be drained from a patient, said first and second bag being arranged at a weighing device for weighing the combined weight thereof.

In order to reduce the total cycle time, the cycler comprises a draining device for draining the spent fluid into the second bag supervised by the weighing device, and a replenishment device for replenishing the first bag at a predetermined replenishment fluid flow rate during said draining step. Preferably, the draining device is a pressure device for generating an underpressure in the pressure chamber comprising

the bags during the draining step. Moreover, the replenishment device may be a volumetric pump arranged at the inlet of the first bag.

The volumetric pump may be arranged to pump the fluid into said first bag at a constant fluid flow rate, whereby the cycler and autoclave is more easy to control. The volumetric pump is arranged to replenish the first bag at a constant fluid flow rate until a predetermined replenishment volume has been introduced into the first bag.

The weighing device is arranged to control the draining step corrected for by the replenishment of the first bag.

The cycler may be arranged to interrupt said draining step when a predetermined volume has been drained into the second bag, or when a predetermined time has elapsed from the start of the draining step. Alternatively, the cycler may be arranged to interrupt said draining step when an inlet flow rate into said second bag is below a predetermined flow rate, said inlet flow rate being determined by said weighing device.

The cycler according to the invention is operated in four phases, in the following order: a drain phase for draining spent dialysate from a patient connected to said second bag; a fill phase for filling the patient with fresh fluid from said first bag; an emptying phase for emptying the spent dialysate in said second bag to a waste receiver; and a replenishment phase for replenishing the first bag with fresh fluid. The replenishment phase and the drain phase takes place at least partially simultaneously. The cycler may be arranged to initiate said replenishment phase during the emptying phase and to initiate the drain phase after the termination of the emptying phase.

In an alternative embodiment the cycler may be operated in the four phases in the following order: a drain phase for draining spent dialysate from a patient connected to said second bag; an emptying phase for emptying the spent dialysate in said second bag to a waste receiver; a fill phase for filling the patient with fresh fluid from said first bag; and a replenishment

phase for replenishing the first bag with fresh fluid. Also in this case, the replenishment phase and the drain phase takes place at least partially simultaneously.

In order that the fluid intended to be introduced into a patient is delivered at a temperature close to body temperature, a heating device is arranged to expose the first bag to heat energy, during said replenishment phase, for heating the fluid in the first bag to a temperature close to 37 degrees Celsius. The cycler is arranged to terminate the replenishment phase and to initiate the fill phase only when the temperature of the fluid in said first bag is close to 37 degrees Celsius.

The cycler may be provided with valves for controlling the fluid flow to and from the first bag and the second bag. There is arranged a first valve for controlling the fluid flow into said first bag from said replenishment device, a second valve for controlling the fluid flow out from said first bag to a patient line, a third valve for controlling the fluid flow into said second bag from said patient line and a fourth valve for controlling the fluid flow out from said second bag. The first valve is opened only when said second valve is closed and vice versa. The third valve is opened only when said second valve and said fourth valve is closed.

The pressure device is arranged to expose said pressure chamber for a positive pressure when the second valve is opened and when the fourth valve is opened, and a negative pressure when the third valve is opened, and either a positive or negative pressure when the first valve is opened.

Alternatively to the volumetric pump, there may be arranged any type of pump, supplemented with a flow meter, which measures the replenishment fluid flow rate of the fluid provided to the first bag. In this manner, the weighing device can be corrected for the replenishment fluid flow rate and thereby obtain full control of the drain fluid flow rate as well as the fill fluid flow rate.

BRIEF DESCRIPTION OF THE DRAWINGS

Further objects, advantages and features of the invention will appear from the following detailed description of several embodiments shown on the drawings.

Fig. 1 is a schematic view of a first embodiment of a device for sterilising a heat sensitive fluid intended to be used according to the invention.

Fig. 2 is a schematic view similar to Fig. 1 of a second embodiment of a device according to the invention.

Fig. 3 is a schematic view similar to Fig. 2 of a portion of a third embodiment of a device according to the invention.

Fig. 4 is a schematic view similar to Fig. 1 of a third embodiment of the device according to the invention.

Fig. 5 is a schematic view of a first embodiment of a cycler which may be connected to the device according to Fig. 2, 3 or 4.

Fig. 6 is a time diagram of the fluid flows in the cycler according to Fig. 5.

Fig. 7 is an alternative time diagram similar to Fig. 6.

Fig. 8 is a schematic view similar to Fig. 5 of a second embodiment of the cycler.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

The fluid to be sterilised comprises a first non-heat-sensitive portion and a second heat sensitive portion. The two portions may be delivered separately to the sterilising device into two separate inlets 1 and 2.

With reference to Fig. 1, the first non-heat-sensitive component, which may comprise sodium chloride dissolved in water, is enclosed in a vessel 3 connected to the inlet 1. The second heat sensitive component, which may comprise glucose, is enclosed in a vessel 4 connected to the inlet 2. The fluid components are preferably provided at a temperature at which each component is relatively stable, such as room temperature.

The first fluid portion from vessel 3 provided to inlet 1 is impelled by a first pump 5 to a heater 6, in which the first

fluid portion is heated to a first high temperature. The second fluid portion is impelled by a second pump 7 and mixed with the first fluid portion in a mixing point 8 arranged downstream of the heater 6. During the mixing, the second fluid portion is rapidly heated to a sterilising temperature, while the first fluid portion is cooled to the same sterilising temperature. The second fluid portion does not make direct contact with the heater surface and so damage is minimised.

In order to promote rapid mixing, the fluids are impelled at such conditions that turbulent flow prevails at least after the mixing point 8. In addition, flow mixing means may be arranged in the flow path, such as at the mixing point 8 or in the flow path downstream of mixing point 8. Such flow mixing means may be flanges or wings in the flow path.

The mixed fluid portions pass through a sterilising tube section 9 dimensioned to provide a predetermined resident or sterilising time for the mixed fluids at the sterilising temperature. The tube section may be insulated as indicated by box 10 to maintain the mixed fluids at the sterilising temperature for the sterilising time. After the sterilising time, the mixed fluids are sterile, since the second fluid portion has been subjected to the sterilising temperature during a sterilising time and the first fluid portion has been exposed to a still higher temperature and still longer time, thus being oversterilised.

The sterilising dose is a function of temperature and time and is defined according to the formula:

$$F_0 = \int_0^t 10^{(T-121)/10}\, dt$$

in which

$F_0$ = the sterilisation dose in minutes
T = temperature
t = time

If the sterilising temperature is 121°C and the time is 20 minutes, a sterilisation dose of 20 minutes is obtained. If the sterilising temperature is 141°C and the time is 12 seconds, a sterilisation dose $F_0$ of 20 minutes is also obtained. A sterilising dose $F_0$ of 20 minutes is considered sufficient, however, in certain applications, a sterilising dose $F_0$ of 10 minutes or even lower may be sufficient.

In the above example, the first fluid portion may comprise sodium chloride at a concentration of 150 mM, sodium lactate at a concentration of 38,8 mM, magnesium chloride at a concentration of 0,56 mM and calcium chloride at a concentration of 1,89 mM. The second fluid portion may comprise glucose at a concentration of 40%, i.e. 400 g glucose per litre solution. The first fluid portion flow rate is 45 ml/min and the second fluid portion flow rate is 5 ml/min. The resulting mixture has the following composition: sodium chloride 135 mM, sodium lactate 35 mM, magnesium chloride 0,5 mM, calcium chloride 1,7 mM and glucose 4%. The first fluid portion is heated from 20°C to 155°C by the heater 6. The second fluid portion is heated from 20°C to 141°C during mixing, while the first fluid portion is cooled from 155°C to 141°C. The resident or sterilising time is 12 seconds resulting in a sterilising dose $F_0$ of 20 minutes. The resulting sterilised fluid mixture is cooled by a cooler 13 and delivered to an outlet 11 and collected in a vessel 12. A pump 20 or other device may be arranged to control the flow to the vessel 12. The sterile fluid may be used as a peritoneal dialysis solution to be delivered to the peritoneal cavity of a patient.

Other medical fluids may be produced by the device according to the invention, such as hemodialysis solutions, infusion solutions used in hemodiafiltration or hemofiltration,

replacement fluids for infusion in the blood, wound irrigation solutions, rinsing solutions etc. Moreover, nutrition solutions often comprises amino acids, which are heat sensitive, and glucose, which is heat sensitive, and cannot be sterilised together with amino acids. Certain drugs, such as insulin, may be produced or included in a fluid administered to a patient, and the drug component may be heat sensitive. Certain medical fluids comprise peptides, proteins or fragments thereof, which normally are heat sensitive. Preservation fluids for blood component handling may also comprise heat sensitive components, at least glucose. In certain cases, glucose is replaced with or complemented with glucose polymers, di-sacharides, tri-sacharides etc. Certain carboxylic acids are heat sensitive and may be included in such fluids. Solutions comprising calcium or magnesium ions and carbonate or bicarbonate ions may precipitate at exposure to a sterilising temperature, and need to be sterilised with the carbonate or bicarbonate separate from the calcium or magnesium containing solution.

In order to control the above procedure, one or several temperature sensors are provided. A first temperature sensor 14 may be arranged immediately downstream of the heater 6 to determine the temperature of the first fluid portion after heating. A second temperature sensor 15 may be arranged between the second inlet 2 and the mixing point 8 to determine the temperature of the second fluid before mixing. A third temperature sensor 16 may be arranged downstream of the mixing point to determine the mixing temperature. A fourth temperature sensor may be arranged downstream of the sterilising section 9 to determine the sterilising temperature. A fifth temperature sensor 18 may be arranged downstream of cooler 13 to determine the temperature of the fluid delivered to vessel 12. Not all of these five temperature sensors are needed so one or several thereof may be excluded.

A control processor 19 may be arranged to control the sterilising device according to the invention. As shown in Fig.

1, the five temperature sensors are connected to the processor as well as the pumps 5, 7 and 20 to provide measurements of the temperatures and flow rates. The pumps 5, 7 and 20 may be volumetric pumps also acting as flow meters. Alternatively, separate flow meters may be provided. The processor controls the heater 6 to provide the required temperature downstream of the heater, as measured by temperature sensor 14, to provide the sterilising temperature after mixing as measured by temperature sensors 16 and 17. The processor calculates the residence time in the sterilising section 9 based on the flow rates of pumps 5 and 7 and the known volume of the sterilising section 9. Finally, the processor may determine the obtained sterilising dose $F_0$.

The control processor 19 may obtain all necessary information in order to calculate the sterilising effect from the flow rates of pumps 5 and 7 and the temperature of sensor 17.

As also shown in Fig. 1, the fluids provided to inlets 1 and 2 may be preheated by preheaters 21 and/or 22.

Since the sterilising apparatus shown in Fig. 1 is intended to heat the fluids to temperatures well above 100°C, it is required to keep the fluids from boiling. This may be done by enclosing the entire apparatus in an enclosure 23, as shown by broken lines in Fig. 1, and raising the pressure inside the enclosure to a pressure sufficient to prevent boiling, such as 3 - 6 Bar absolute pressure. Another method would be to arrange a high pressure zone in the pipes or lines between pumps 5, 7 and 20.

It is known that glucose decomposes when exposed to heat, and is thus a heat sensitive component of the fluid. Glucose also decomposes during storage. It is known that several factors influence the decomposition of glucose, among which are pH, temperature, time, glucose concentration and mixing with certain ionic components. Glucose decomposes into components, some of which may be more or less toxic or are able to induce toxic reactions by including precursors for such reactions. If the resulting fluid is to be used as a medical fluid for infusion

into a human being or other mammal, the toxic components or precursors should be minimised.

In order to sterilise the fluid it is necessary to expose the fluid to sterilising conditions. There are several methods available, such as heat sterilisation (autoclaving), filter sterilisation and other methods. The present invention is limited to heat sterilisation.

During heat sterilisation, it is known that decomposition of glucose can be minimised if glucose is sterilised during a short time at a high temperature. The rationale is that the decomposition reaction is less sensitive to high temperature than the sterilising reaction.

In order to minimise the decomposition before sterilisation, it is advantageous to store the fluid at a low pH and at a high concentration, which is suggested according to the invention. The pH may be from 2,6 - 5,0 and preferably pH=3,2. The concentration may be above 15% or above 20% with 40% - 50% being preferred, calculated as weight of glucose per litre solution.

The sterilisation may take place during a short time and at a pH of below about 5,5 and at a dilution concentration. It is believed that the short time is of greater importance than the other factors for avoiding decomposition into toxic components of glucose during the sterilisation process.

It is also recognised that glucose may decompose into precursors for AGE, advanced glucosylation end products. When a glucose solution comprising precursors for AGE contacts proteins in the body, a non-enzymatic reaction takes place resulting in AGE formation. The long term effect of AGE is still not well known. Gentle heat sterilisation of glucose as suggested in the present invention is expected to reduce the level of glucose degradation products of the type of AGE precursors.

An alternative embodiment of the invention is shown in Fig. 2. In this embodiment the sterilising device according to the invention is integrated in a PD monitor arranged to provide a PD solution to a patient. The PD solution is prepared from two

concentrates provided in two concentrate bags 51 and 52 and connected to concentrate input connectors 56 and 57, and a supply of pure water, for example provided from a reverse osmosis RO-unit 53 connected to a water input connector 58 for connection to a potable water supply. The sterilised PD fluid is delivered to a PD cycler 55, which is, in turn, connected to a PD fluid output connector 59 for delivery to the patient.

Each of the three input connectors and the output connector may be arranged as a heat sterilisable connector. Such a heat sterilisable connector device is described in WO 96/05883, which is enclosed in the present specification by reference.

Each of the inputs 56, 57 and 58 and the output 59 is arranged as a connector device. Input 56 is arranged to connect a first concentrate bag 51 to a first metering pump 60 and input 57 is arranged to connect a second concentrate bag 52 to a second metering pump 61. Input 58 is connected to RO-unit 53 and a third pump 62 is arranged to pump pure water from RO-unit 53.

Pumps 62 and 60 are driven to mix the concentrate from bag 51 with pure water from RO-unit 53 to provide a desired concentration. A conductivity cell 63 may be arranged to measure the conductivity of the mixture and may control the pump 60 and/or 62 to obtain the required conductivity and thus the desired concentration. Pump 62 is preferably driven to provide a constant flow of for example 54 ml/min and at the same time increase the pressure to 3 - 6 Bar absolute pressure to avoid boiling during sterilisation. The fluid provided so far is the first heat-insensitive fluid mentioned above.

The first fluid passes through a first heat exchanger 64 comprising a primary circuit 64a for heating the first fluid, for example from 20°C to 100°C. Then, the first fluid passes through a heater 65 such as an electric heater powered by an electric power supply 66 to heat the first fluid to a temperature of 155°C.

The second, heat sensitive, fluid from bag 52 is pumped by pump 61, at a flow rate of 6 ml/min to a mixing point 67

immediately downstream of heater 65 to mix with the first fluid. The second fluid is thus rapidly heated from room temperature to a temperature of 141°C by being mixed with the hot first fluid, which at the same time cools down to 141°C.

Then, the mixed fluids pass through a sterilising unit 68 comprising a tube 68a of a length suitable for providing a residence time giving the required sterilising time, such as 12 seconds. The tube is embedded in an insulating material 68b to minimise the temperature decrease during the residence time.

Immediately downstream of the sterilising unit 68 is a temperature sensor 69, which controls the power supply 66 so that the temperature is the desired sterilising temperature, such as 141°C.

Pump 61 is controlled to deliver the heat sensitive fluid in the amount desired. For example, if the heat sensitive fluid is glucose at a concentration of 40%, the flow rate should be 6 ml/min to give a final concentration of 4% if the first flow rate is 54 ml/min. If a concentration of 1,5% is desired, the flow rate should be 2,1 ml/min and if a concentration of 2,5% should be obtained, the flow rate should be 3,6 ml/min. In each case, the temperature sensor adjusts the power supply to heat the first fluid to a suitable temperature so that the sterilising temperature is obtained.

After the sterilising unit 68, the now sterilised fluid enters the secondary circuit 64b of the heat exchanger 64 to rapidly decrease the temperature of the sterilised fluid, for example to 60°C. Then, the sterilised fluid passes a flow restrictor 70 to decrease the pressure to close to atmospheric pressure. Preferably, the flow restrictor 70 is controlled by a pressure sensor 71, so that the pressure before the restrictor is the desired pressure to prevent boiling, such as 6 Bar absolute pressure.

From the flow restrictor 70, the sterilised fluid is delivered to the output 59, which is connected to a PD cycler 55. A pressure relief valve 72 is arranged to connect the sterilised

fluid to a waste 73 if the pressure of the fluid exceeds a predetermined value, such as 150 mmHg above atmospheric pressure.

The PD cycler may be of the type described in WO 95/20985, comprising a pressure chamber. A disposable line set is connected between the outlet connector and the patient and comprises a heater bag and a drain bag, a drain line and a supply line. The heater bag and a drain bag are arranged on a weighing device, such as a pair of scales. Four valves in a valve unit are arranged to operate on the drain and supply lines. Finally, the line set comprises a PD patient connector for connection to a catheter ending in the peritoneal cavity of the patient. The PD replenishment fluid from outlet 59 is supplied to the heater bag via the valve unit until the scales indicate that the heater bag has been replenished to a predetermined volume, such as 3 litres. Then the patient is drained by exposing the pressure chamber to a subpressure to withdraw fluid in the peritoneal cavity of the patient out via the open valve unit into the drain bag. The combined weight of heater bag and drain bag is weighed and the drain phase is terminated when it is determined that the drain flow rate is below a predetermined limit or a drain time has elapsed. The drain flow rate is determined by means of the weighing device. Then, the pressure chamber is exposed to an overpressure and the valve unit is opened to allow the replenished and sterilised PD fluid to flow into the peritoneal cavity of the patient. The flow rate and the delivered fluid volume is monitored and the fill phase is terminated when a desired fill volume has been delivered. The temperature of the heater bag is controlled by a heating device and temperature sensor so that the fluid delivered has a temperature of about 37°C. Finally, the drain bag is emptied to a waste receiver by opening the valve unit and exposing the pressure chamber to an overpressure.

When the patient has been exposed to a fluid exchange as described above, the PD fluid is left in the peritoneal cavity for a dwell time until the next exchange cycle. During the dwell,

the sterilising device provides new replenishment sterile fluid to the heater bag. It takes about 33 minutes to produce a volume of 2 litres if sterile fluid is produced at 60 ml/min.

It may be desirable to include a cooler 82 after the flow restrictor 70 to further decrease the temperature before delivering the fluid to the heater bag. The cooler may be a Peltier cooler or a heat exchanger of conventional design, using cold water or a cooling medium as heat energy absorption medium. A cooler 91, such as a Peltier cooler, may alternatively or additionally be placed after residence device 68 and before heat exchanger 64, in order to rapidly cool the heat sensitive mixture to a safe temperature, such as from 141°C to 120°C. In this way, the heat sensitive component is heated rapidly from room temperature to sterilisation temperature of 141°C at mixing point 67, is maintained at the sterilising temperature during 12 seconds by residence device 68 and is then rapidly cooled to 120°C by Peltier cooler 91 and then further cooled to room temperature in the slightly slower heat exchanger 64.

The sterilising device needs to be disinfected at suitable intervals, for example once per day or once per week. For that purpose, the side openings of the connector devices 56, 57, 58 and 59 are used. The side opening 83 of RO inlet 58 is connected to the side opening 82 of outlet 59 via a line 84. The side opening 85 of first inlet 56 is connected to the flow line 86 between RO inlet 58 and the pump 62 via a line 87. The side opening 88 of second inlet 57 is connected to the line 89 between heater 65 and sterilising unit 68 via a line 90.

During disinfection, the sterilising device is filled with pure water obtained from the RO-unit. Then, connectors 57, 58 and 59 are disconnected from the respective sources.

Thus, the RO-inlet connector 58 and the outlet connector 59 are connected via line 84 and side openings 82 and 83. The second inlet connector 57 is in the same position so that a circulating path is obtained via pump 61, line segment 89, line 90, side opening 88 and inlet 57. A disinfecting solution is provided in a

vessel connected to the first inlet 56. The disinfecting fluid may be sodium carbonate, citric acid or any other known disinfection fluid. Pumps 62 and 61 are operated to circulate the fluid in the circuits. Finally, pump 60 is operated to infuse disinfection fluid into the water until a sufficient disinfectant concentration has been obtained. The surplus water is rejected via relief valve 72 to the waste receiver 73. Pump 62 circulates the disinfection fluid through the complete sterilisation device and the outlet 59 is connected to the inlet 58 via line 84 to complete the circuit. The disinfection fluid may be left in the machine until the next use. Before the next use, the machine is rinsed with pure water via inlet 58 from the source of RO-water.

Descaling with citric acid or other descaling agent is performed in the same manner.

In order to avoid dripping from the connectors, the inlet connectors 56, 57 and 58 and the outlet connector 59 are positioned at the highest position of the flow path and at the same level.

The machine may be emptied by opening all inlets 56, 57 and 58 and the outlet 59 and by opening the relief valve 72, which is positioned at the lowest point of the flow path and allowing air to enter all lines and devices.

During chemical disinfection and/or descaling, the heater 65 may be turned off or adjusted to heat the fluid to a low temperature. The flow restrictor 70 may be opened.

In heat sterilisation, the fluid in the entire circuit is heated to 121°C and circulated for at least 20 minutes to obtain sterilisation of the entire circuit. In this case, pressure relief valve 72 is operated to permit a pressure of 2 Bar, thereby preventing boiling of the water in the circuit at 121°C.

The same or a similar procedure may be used for sterilising the flow path of the sterilising device. The fluid circuit is arranged for a treatment with all connectors inserted in respective bore in the non-engaged position. The circuit is full with water, which is circulated by pump 62. Flow restrictor 70 is

opened and relief valve 72 is adjusted to a pressure of 2 - 3 Bar absolute pressure. First inlet connector 56 is operated to connect the vessel 51 to the circuit. Then, pump 60 is operated to introduce some fluid (electrolyte fluid) in the circuit until the pressure reaches about 2 - 3 Bar absolute pressure. Since the fluid circuit is relatively non-compliant, the volume of fluid introduced is small. Then, the heater is activated to heat the water present in the circuit to a temperature of 121°C and the circulation continues for 20 minutes or longer, until sterilisation is obtained. Pump 61 is operated simultaneously to sterilise the circuit comprising inlet connector 57.

After sterilisation has been obtained, RO inlet 58 is activated to connect RO-unit 53 to the circuit and at the same time disconnect bypass line 84. Pump 60 is stopped, and heater 65 is activated. Flow restrictor 70 is activated and pressure relief valve 72 is adjusted to the normal value of 150 mmHg overpressure. Thus, sterile water is produced and delivered to the waste 73 via relief valve 72. Then, the second inlet is activated to connect vessel 52 and pumps 60 and 61 are operated to provide a PD fluid. When stable conditions are obtained, the outlet 59 is activated to deliver sterilised fluid to the heater bag.

In some cases, the heat sensitive component may be introduced together with the remaining components, and the bag 52, connector 57 and the corresponding pump 61 can be dispensed of. Instead, the other components of the fluid may be entered in the same way as component 51, i.e. mixed with water and the remaining components before heat sterilisation.

During the drain and fill phases of the PD cycler, the sterilising device may continue to produce PD fluid. However, since the valve unit is closed, the PD fluid produced is directed to the waste receiver 73 via relief valve 72. Since the drain and fill phases may last up to 20 minutes or more, a considerable amount of PD fluid is wasted. To minimise such waste, pumps 60 and 61 may be stopped during the periods when the heater bag is

not being filled, and the sterilising device is only producing and wasting sterile water.

The first and/or second concentrates may comprise the same substances or components as mentioned above, however, with the contents of the first vessel 51 concentrated by omitting some of the water. The contents of the first vessel may be concentrated for example 30 - 40 times.

In an alternative embodiment, the PD fluid is intended to comprise bicarbonate instead of or in addition to lactate. Calcium cannot be included in the same vessel as bicarbonate, because of the risk of precipitation of calcium carbonate. In that case, the calcium chloride may be included in the second vessel 52 in a suitable concentration. The calcium concentration will then be proportional to the glucose concentration, which may result in a calcium neutral PD fluid. Another advantage of including the calcium ions in the second vessel is that scaling of the pipe system is avoided before the mixing point 67, and the requirement for descaling would decrease.

Further components may be included into the fluid flow before pump 62, by the inclusion of a further bag 51a, connector 56a and pump 60a, in parallel with vessel 51.

Each of the sterilisable connectors may be replaced by a conventional connector device and a three way valve of conventional type, as shown in more detail in Fig. 3, which shows an alternative embodiment of the invention.

Fig. 3 shows an alternative design of a mixing system delivering the mixed fluids in parallel through the residence device. Fig. 3 shows only the right-hand portion of Fig. 2 to the right of pump 62 and pressure sensor 70. The left-hand portion may be identical to the embodiment of Fig. 2. The same components as in Fig. 2 have received the same reference numerals but adding 100 to the reference numbers. Thus, there is shown a heat exchanger 164 comprising a primary circuit 164a and a secondary circuit 164b and a pump device 164c. An electrolyte solution or pure water is conducted through line 189 through heat exchanger

primary circuit 164a and a second heater 165, for example an electric heater controlled by a temperature sensor 169.

A first bag 152a comprising a heat sensitive first component such as glucose is connected via a connector 192a to a three-way valve 157a. The first component passes from the three-way valve 157a to a pump 161a and further to a mixing point 167a, in which the first component is heated to 141°C by mixture with a heated electrolyte component, having a temperature sufficient for promoting such heating by mixing, the temperature being for example 155°C. The mixing temperature is controlled by a temperature sensor 169a, which operates a throttle valve 193a arranged before the mixing point 167a. By throttling the valve 193a, a sufficient flow rate for obtaining said temperature is adjusted.

A second bag 152b comprising a heat sensitive second component, such as amino acids, is connected via a connector 192b to a three-way valve 157b. The second component passes from the three-way valve 157b to a pump 161b and further to a mixing point 167b, in which the second component is heated to 141°C by mixture with a heated electrolyte component, having a temperature sufficient for promoting such heating by mixing, the temperature being for example 155°C. The mixing temperature is controlled by a temperature sensor 169b, which operates a throttle valve 193b arranged before the mixing point 167b. By throttling the valve 193b, a sufficient flow rate for obtaining said temperature is adjusted.

The two heat sensitive components heated to sterilising temperature by mixture with the electrolyte component are handled in parallel in two separate lines 194a and 194b, which pass in parallel through the residence device 168, the pre-cooler 191, if present, and to heat exchanger secondary circuit 164b. After cooling in the heat exchanger, the two fluids are mixed in a Y-connector 195 before entering the restriction device 70, see Fig. 2. The bags 152a and 152b are weighed and when a sufficient amount of fluid has been taken out from each bag, valve 157a

and/or valve 157b are switched to stop the flow of first and/or second components from bags 152a, 152b, respectively.

During sterilisation, the three-way valves 157a and 157b are connected according to the broken lines in Fig. 3, in order to pass fluid, by means of pumps 161a and 161b in the fluid lines to and from the three-way valves 157a and 157b via lines 190a and 190b.

It is realised that more than two heat sensitive components may be handled in parallel by adding further bags 152 and further lines 194. Of course, the same procedure may be adopted for components which are less heat sensitive, to obtain a simple system, whereby the electrolyte component may be replaced with pure water, and thus, the electrolytes may be added one by one or several at a time.

A further alternative embodiment of the invention is shown in Fig. 4. From the left, the device 100 comprises a connector 101 for connection to a source of pure water, such as an RO-unit (not shown). The device further comprises three concentrate connectors 102, 103 and 104, which may be integrated into a single connector device. Each of connectors 102, 103 and 104 connects to a vessel or bag comprising a concentrate, such as a first bag 105 comprising a concentrated bicarbonate solution, a second bag 106 comprising electrolytes, such as sodium chloride, magnesium chloride, calcium chloride, and sodium lactate, at a predetermined pH, and a third bag 107 comprising glucose at a concentration of 50%. Of course, the bags include the components necessary for the final solution as discussed in more detail below. The components are divided into separate bags because they cannot be stored together or they cannot be sterilised together, or for other reasons.

Alternatively, one or more of the vessels or bags 105, 106, 107 may comprise a powder instead of a solution in which case appropriate dissolution means may be provided.

Conveniently, the bags 105, 106 and 107 are combined into a single assembly. The combined assembly of bags is attached to a

weighing device 108, so that the weight of the assembly is monitored. The connectors 102, 103 and 104 are attached to the ends of flexible tubes of PVC or other suitable pliable material, so that the connectors and tubes do not significantly influence the weight of the assembly.

The RO inlet connector 101 is connected to a line system including a first inlet line 109. Inlet line 109 is provided with an inlet valve 110, to isolate the device 100 if required. Inlet valve 110 is normally closed, but is opened upon activation by a control device 111 shown by broken lines. The control device may be a computer or microprocessor or any other control device. Normally, it is the control computer of the complete device.

Inlet line 109 further comprises a heater 112 and a temperature sensor 113, which operate together to adjust the temperature of incoming pure water to a predetermined temperature of e.g. 25°C, in order to make the device independent of incoming water temperature.

Inlet line 109 further comprises a flow meter 114 for measuring the complete inlet flow through inlet connector 101, for a purpose to be described later.

Downstream of flow meter 114, inlet line 109 is divided into water line 115 and concentrate line 116. Water line 115 comprises a first pump 117 for increasing the pressure of the water in water line 115 downstream of the pump to a pressure of 2 - 6 Bar absolute pressure. The pressure is measured by a first pressure sensor 118 and monitored by a second pressure sensor 119. The first pressure sensor 118 is connected to the control system of computer 111, while the second pressure sensor 119 is connected to a parallel supervising system for ensuring the safety of the system. Several of the sensors are duplicated in this manner to provide independent data to the supervisory system or processor, even if not explicitly indicated in the drawings.

Water line 115 further comprises a valve 120 and a primary circuit of a heat exchanger 121. In the heat exchanger, the water in water line 115 is heated from about 25°C to about 131°C in

heat exchanger 121, at a flow of about 120 ml/min. The temperature of the heated water is monitored by temperature sensor 122. Finally, water line 115 comprises a second heater 123, for heating the water to a still higher temperature, such as about 145°C. The hot water is delivered to a mixing point 124.

In concentrate line 116, there is a valve 125 for connecting the normally closed concentrate line 116 to water line 115. Further downstream, concentrate line 116 comprises three concentrate valves 126, 127 and 128 and a reversible second pump 129. The second pump 129 is arranged to withdraw concentrate solutions or fluids from any one of concentrate bags 105, 106 or 107 depending on the positions of valves 126, 127 and 128. The second pump 129 further increases the pressure of the fluid in concentrate line 116 to a pressure of 2 - 6 Bar absolute pressure.

Downstream of second pump 129 is arranged a valve 130, and therefrom, the concentrate fluid is delivered to a second primary circuit of heat exchanger 121 in order to preheat the concentrate solution from e.g. room temperature to about 131°C. From heat exchanger 121, the concentrate solution is delivered to mixing point 124.

Upstream of the second pump 129 is arranged a temperature sensor 131 for measuring the temperature of the incoming concentrate fluid, and downstream of the second pump is arranged a pressure sensor 132 for measuring that sufficient pressure has been obtained. As indicated before, these sensors may be duplicated for supervisory purposes.

In mixing point 124, the two fluid lines 115 and 116 are joined so that the heated water in line 115 is mixed with preheated concentrate in line 116, and the mixture is transported in mixed fluid line 133. Mixed fluid line 133 comprises a residence device 134, normally being a length of tube of a length to produce a predetermined residence time at a predetermined rate of flow to effect sterilisation of the fluid in the residence device 134. The residence device 134 is preceded by a temperature

sensor 135 and followed by a temperature sensor 136. These temperature sensors control the heater 123 to ensure that sterilising conditions are obtained in the residence device 134, such as a minimum temperature of 141°C for 12 seconds.

From the residence device 134, the sterilised and mixed fluid is passed to the secondary circuit of heat exchanger 121, at a temperature of approximately 141°C. The sterilised fluid is rapidly cooled to about 37°C.

Downstream of the heat exchanger, mixed fluid line 133 comprises sterilised fluid at a temperature suitable to be delivered to a patient or a storage bag. The temperature is monitored by a temperature sensor 137. Finally, a valve 138 directs, when activated, the fluid to an outlet connector 139, via a restrictor device 140, for lowering the pressure to atmospheric pressure.

The restrictor device may be a small hole in a piece of metal, the hole being dimensioned to reduce the pressure from 6 Bar to 1 Bar at the desired flow rate of, for example, 140 ml/min. An alternative design would be to use a controllable throttle valve, which is controlled by the processor in dependence of pressure sensor readings. A third alternative would be to use a throttle device or the pressure relief type, which adjust the differential pressure over the throttle device to a predetermined pressure drop of, for example, 5 Bar. A fourth alternative would be to use a throttle device controlled to deliver fluid at an output pressure of no more than a predetermined safe pressure of, for example, 1.25 Bar, in which case the pumps are operated to ensure that the pressure before the throttle device is sufficiently high, for example 6 Bar.

It is noted that the on-line autoclave as described is always operated at a predetermined minimal flow rate of not less than a predetermined flow rate, for example 120 ml/min, in order to ensure that the autoclave is maintained sterile. As soon as the flow rate drops below said predetermined minimum flow rate, the sterility conditions may be hampered or the autoclave may not

be controlled to operate at proper temperatures. The autoclave may be designed to operate at different flow rates above said minimum flow rate. In order to always maintain a minimal flow rate, any excess fluid produced may be sacrificed to the waste.

If the mixed and sterilised fluid cannot be delivered out via the output connector 139, a valve 141 is activated to deliver the fluid to a waste receiver via a waste line 142. Waste line 142 further comprises a primary circuit of a second heat exchanger 143, a pressure sensor 144, a restrictor device 145 and a valve 146 until the fluid is delivered to the waste receiver 147. A temperature sensor 148 arranged upstream of heat exchanger 143 and another temperature sensor 149 arranged downstream of valve 146 are used to measure the temperatures of the waste fluid.

The device according to Fig. 4 may be operated in different modes. One mode of operation will be described below, namely sequential delivery of the components of the final fluid. It is, however, understood that the device may operate as described in connection with Fig. 2 as well.

In the sequential operation mode, water is first delivered in inlet line 109 at a constant rate of 120 ml/min from inlet connector 101, via flow meter 114, in which the flow rate is monitored, and via water line 115 and via first pump 117 to raise the pressure so that the boiling temperature of the fluid is above the temperature anywhere in the circuit. If the maximum temperature is about 150°C, the pressure should be above 4.8 Bar or preferably about 6 Bar absolute pressure. The exact pressure is dependent on the adjustment and operation of restriction device 140. The water further passes the mixing point 124 and enters the mixed fluid line 133 and reaches valve 138, which directs the flow to waste line 142, via valve 141 and further to the sump. The outlet connector 139 is connected to a recipient, normally a bag, such as a heater bag described below.

When all conditions are checked and the device delivers sterilised water, valve 138 is switched to direct the sterilised water to the outlet connector 139 via restrictor 140.

Substantially at the same time, or shortly thereafter, valve 127 in concentrate line 116 is opened and concentrate pump 129 is activated, with valve 130 in an open condition, to pump concentrate fluid from electrolyte bag 106, via heat exchanger 121 to mixing point 124. The concentrate pump 130 is operated to provide a flow rate of approximately 20 ml/min. At the same time, the weight of the concentrate assembly is monitored by weighing device 108. If the intention is to provide 1 litre of final solution and the concentrate fluid in bag 106 has a concentration of 1:40, the flow is continued for about 1 minute and 15 seconds, until the weighing device indicate that a volume of 25 ml has left the bag 106, whereby 25 ml is the amount required from concentrate bag in 1 litre of final fluid (1:40).

Then, valve 127 is switched off and valve 125 is opened for a short time, such as 15 seconds, to rinse the concentrate line 116.

For including the second concentrate, which may be glucose, bag 107 is connected to the concentrate pump by closing valve 125 and opening valve 128. If the glucose concentrate fluid has a concentration of 50%, the concentrate pump is driven 1 minute per percent concentration to be required in the final fluid at 20 ml/min. If 4% is required, which is the maximum contemplated for a PD fluid, the glucose concentrate is dosed in 4 minutes.

After this step, the concentrate line 116 is again rinsed with water, for example for 15 seconds.

Thereafter, the bicarbonate bag 105 is connected. The bicarbonate is normally stored at a concentration of about 1000 mmol/l. First, valve 125 is closed and valve 126 is opened so that concentrate pump 130 pumps bicarbonate fluid out of bag 105. The flow rate may be the same, 20 ml/min, and the mixing and sterilisation of bicarbonate fluid is discontinued when the weighing device determines that the required quantity has been

removed from bag 105. If the final solution should contain 15 mmol/l, the concentrate pump is operated for 45 seconds to take 15 ml of concentrated bicarbonate solution out of bag 105.

Finally, the concentrate line is rinsed once again and water is delivered to the outlet connector, until the final volume of fluid has been delivered to the bag connected at the outlet connector, which is determined by flow meter 114 in combination with the weight losses measured by weighing device 108 and calculated into volumes by computer 111, taking into account the different densities of the concentrate fluids.

This final filling of water also means that the mix of fluid in the bag connected to the outlet connector is agitated and mixed thoroughly.

During the complete sterilisation process described above, valves 138 and 141 are maintained in the same position directing all fluid to the outlet connector 139. Thus, all fluid produced is delivered to the receiver, thereby minimising the time required for the preparation of the complete fluid.

Thus, it is also evident that all fluid exiting from the concentrate bags 105, 106 and 107 is finally delivered out of connector 139, so that there is no waste of concentrate fluid.

In the example above, 1 litre of final solution has been prepared, but in PD it is more normal that 2 litres are generated each time, or any other volume as required by the user. It is understood that 2 litres may be produced by doubling the above-mentioned times or by repeting the production of 1 litre two times.

It is contemplated that the concentrate fluid bags may include concentrate fluid required for a final fluid volume of 12 - 25 litres or more if required. Then, the above sequence is repeated for each batch of 2 litres to prepare.

In certain applications for PD, bicarbonate is not used, but lactate is used as the sole buffer. In that case, the third bag in the concentrate assembly is unnecessary, and only two bags may be used. In that case, valve 126 is always closed.

To prepare one batch of 1 litre (1,5% glucose concentration), takes about 7 minutes and 45 seconds, supposing that the RO unit delivers pure water at 120 ml/min and 25 ml electrolytes, 15 ml bicarbonate and 30 ml glucose are used. Thus, the waiting time between each PD exchange of about 2 litres has to be more than 15,5 minutes. This might be limiting in some circumstances as appears from an explanation of the drain and fill phases of a PD treatment below.

In Fig. 5 is schematically shown a PD cycler 200 intended to be used in the present invention. The PD cycler comprises a pressure chamber 201 enclosing a heater bag 202 and a waste bag 203. The heater bag 202 is connected to the outlet connector 139 of fluid sterilisation device 100 of Fig. 4 for receiving a fresh sterilised fluid for introduction into heater bag 202. Heater bag 202 is connected with connector 139 via a first tube 204 ending with a connector 205 mating with connector 139 and comprising a valve 206. A second tube 207 connects heater bag 202 with a connector 208 to a patient (not shown) and the second tube 207 is controlled by a second valve 209. A third tube 210 connects the patient connector 208 to the drain bag 203 via a third valve 211. Finally, a fourth tube 212 connects drain bag 203 with a waste line 213 via a valve 214. Heater bag 202 and drain bag 203 rest on a pair of scales 215 which monitor the combined weight of the two bags.

The operation of the PD cycler as schematically disclosed in Fig. 5, appears from the diagrams of Fig. 6 or 7. The diagram indicates the fluid volumes of the heater bag and drain bag during the different phases.

After priming, which is more closely described below, the first phase of the treatment is a drain phase, at the start of which the heater bag is full of fluid, normally about 2,5 litres, and the drain bag is empty. The patient is connected and the third valve 211 is opened and a subpressure is exerted in pressure chamber 201. Fluid is withdrawn from the patient into drain bag 203 at a flow rate depending on the patient catheter

and the subpressure, normally from 150 - 300 ml/min. When the peritoneal cavity of the patient is almost empty, which may be indicated by a decrease of the drain flow as measured by the scales 215, the drain phase is terminated. The drain phase is normally 7 - 10 minutes.

The second phase is a fill phase, in which the peritoneal cavity of the patient is filled with fresh fluid contained in heater bag 202. An overpressure is exerted in pressure chamber 201 and valve 209 is opened, while the other valves are closed. The fill flow rate depends on the patient and the overpressure and may be 150 ml/min. The fill phase is normally 10 - 15 minutes.

The third phase is an empty drain bag phase, in which an overpressure is exerted in the pressure chamber 201 and valve 214 is open. The fluid in the drain bag is directed to a waste line 213. The volumes are always monitored by the scales 215. The third phase may be about 2 minutes, since a high overpressure may be used and the flow restriction is minimal.

The fourth phase is heater bag replenishment phase with valve 206 open. In this case, normally a subpressure is exerted in the pressure chamber 201. Fluid is received from the sterilising device 100 connected to connector 205 at a flow rate of about 120 ml/min. The fourth phase is normally 15 - 17 minutes.

Thus, a complete cycle is 34 - 44 minutes. During a night treatment of 8 hours, it is possible to exchange 22 - 28 litres, in batches of 2 litres.

As shown in Fig. 7, the emptying phase and the replenishment phase may be interchanged.

If it is desired to increase the fluid volume further, the times in the different phases have to be shortened. It is noted that the heater bag fill time of 15 - 17 minutes could be shortened by increasing the flow rate of fluid from steriliser 100. However, increasing the flow rate means considerable cost increases.

Instead it is noted that the flow rate of the fluid delivered from steriliser 100 is monitored by the steriliser by flow meter 114 and weighing device 108. Thus, it is possible to replenish the heater bag during (part of) the drain cycle as shown in Figs. 6 and 7. This is done by opening valve 211 while valve 209 is closed during the heater bag replenishment phase. If the drain phase is terminated before the heater bag is replenished, the patient fill phase cannot start until the heater bag replenishment is completed. However, it is no drawback to continue the drain phase longer, since that only results in some further fluid being drained, which normally is an advantage. Since the replenishment flow from the steriliser is known, the PD cycler still has full control of the flows by using the reading from the scales and subtracting the replenishment flow obtained from the steriliser. In this way, almost the complete drain phase can be saved in the cycle time, i.e. up to 10 minutes.

In Fig.6, the normal cycle time is shown by arrow 216 while the shortened cycle time according to the invention is shown by arrow 217. In Fig. 7, the normal cycle time is shown by arrow 218 while the reduced time according to the invention is shown by arrow 219. In fact, the two cases of Figs. 6 and 7 becomes the same according to the present invention, see arrows 217 and 219.

In Fig. 7, it is shown that the replenishment phase starts immediately after the fill phase. However, it is understood that it can start any time during the emptying phase or the following drain phase. However, by starting the replenishment phase as soon as possible, longer time is obtained for heating the replenishment fluid to 37 degrees Celsius.

In Figs. 6 and 7, the pressure in the pressure chamber is indicated at the bottom by "neg" and "pos", indicating a subpressure or an overpressure. Since the replenishment phase does not need a negative pressure, there is only one positive period and one negative period of pressure in a cycle, compared to two of each in the normal cycle of Fig. 7. This will result in a saving of the power required for the air pump in the cycler and

a reduction of the sound level. The replenishment takes place by means of the volumetric pump and overpressure in the autoclave, possibly monitored by a flow meter, such as flow meter 220 shown in Fig. 5.

In this operation mode, it is still possible to keep accurate control over the ultrafiltration, since the volume of fluid drained from the patient and the volume of fluid filled into the patient are under full control of the mass balance device 215.

If the cycle time needs to be further shortened, that is possible by the addition of a storage bag in the line set as indicated in Fig. 8. It is noted that the steriliser has to direct the sterilised fluid to the waste 147 during the second phase filling the patient, when valve 206 is closed, as well as under the third phase emptying the drain bag.

In Fig. 8, the same components as in Fig. 5 have received the same reference numeral starting with 3 instead of 2. The inlet tube 304 is provided with a branch line 316 ending in a storage bag 317. When valve 306 is closed during the first, second and third phase, the steriliser 100 delivers PD solution into storage bag 317 via tube 316. The heater bag 302 may then be replenished much faster from the storage bag 317 compared to the embodiment of Fig. 5. Thus, the heater bag replenishment phase may be reduced to 2 minutes or less. The efficiency of the complete device becomes dependent only on the cycler and its capacity to drain and fill the patient. The surplus time is merely 4 minutes, 2 minutes for emptying of the drain bag and 2 minutes for replenishment of the heater bag. The procedure has to be controlled if the steriliser is operated in the sequential mode as described in connection with Fig. 4, since the filling of heater bag has to start only when the concentrations are correct in storage bag 317, i.e. after the completion of an entire fill cycle from the steriliser.

The storage bag may also be used as an entry point for addition of medicaments or other additions, like insulin, antibiotic drugs, potassium chloride etc.

It is recognised that the PD solution produced according to the steriliser in Fig. 4 will produce sterile bicarbonate fluid and enter it in the storage bag 317, and then produce sterile glucose solution and subsequently enter that in the storage bag 317. Since the glucose fluid has a low pH, some of the bicarbonate will react and form carbon dioxide, which may be released as a gas. Thus, storage bag 317 is provided with a valve and tube arrangement 318 to indicate when there is surplus gas in the storage bag 317 and expel it to the atmosphere. Another means for doing the same would be to include a sterile filter or hydrophobic filter at the top of storage bag 317. The gas may be expelled in a time interval when outlet valves 138 and 140 are opened (the position shown in Fig. 4) and pressure chamber 301 has an overpressure and valve 306 is open to exert an overpressure into storage bag 317 and expel gas therein.

In the above example indicated in connection with Fig. 4, the bicarbonate concentrate was sterilised at a concentration of about 140 mmol/litre(1000x20/140). However, there is a risk that carbon dioxide is formed during heat sterilisation at such a concentration, and thus, the concentrate pump may be operated at a lower speed during sterilisation of bicarbonate fluid.

In Fig. 4, the concentrate fluid is preheated to quite a high temperature. This is performed in an efficient heat exchanger 121 in which the heating fluid is the final sterilised fluid in the secondary circuit of the heat exchanger. Thus, the heat exchanger cannot have any point with higher temperature than the sterilising temperature, and decomposition of the heat sensitive component is minimised. The further heating to the final sterilisation temperature, i.e. from about 131°C to about 141°C takes place by the method of mixing with a fluid having a slightly higher temperature. Thus, the heat sensitive fluid component is never exposed to harsh conditions, such as hot

points having excessive high temperatures, as may appear in an electric heater 123. Thus, favourable conditions for less formation of degradation products are obtained. The temperature difference between the primary and secondary circuits of the heat exchanger is about 10°C, which is possible to obtain without excessive long residence times in the heat exchanger.

In Fig. 4, there is a circuit not previously described for sterilising the equipment before use. In water line 115, a parallel circuit to valve 120 and heat exchanger 121 is arranged comprising valve 150 and the primary circuit of heat exchanger 143. When heat disinfection of the complete steriliser 100 is to be performed before a treatment, valve 120 is closed, valve 150 is opened and heater 123 is operated. The water passes from pump 117 via valve 150 to heat exchanger 143 and further to heater 123 to be heated to a temperature of, for example, 141°C. The hot water passes heat exchanger 121 but is not cooled appreciably since the primary circuit of exchanger 121 is disconnected and has no flow. The hot water after heat exchanger 121 passes through line 133 and via valves 138 and 141 to heat exchanger 143 to give off its heat to the water passing at the primary side thereof. Finally, the water is discharged to the waste via restrictor device 145, which lowers the pressure from about 2 - 6 Bar to atmospheric pressure.

Thus, the on-line autoclave is self-sterilised and is ready for producing PD fluids. The self-sterilising step may be performed in about 30 minutes and is initiated under program control to happen shortly before the start of a PD treatment, which is scheduled in advance by a patient. When the self-sterilisation process is ready, the machine awaits the arrival of the patient, which connects a disposable set, such as set 200 or 300 to the outlet connector 139. Then, the device produces a quantity of sterile treatment fluid into heater bag. However, before the patient is connected to connector 208, the tubes should be filled with fluid to displace the air therein. This is performed by attaching the connector 208 to a hook or attachment

device on the cycler at approximately the same level as the heater bag. Then, valve 209 is opened to allow fluid to flow through tube 207 to patient connector 208. Then, the connector 208 is ready for connection to the patient.

It is appreciated that the priming procedure described above takes about 20 minutes, since the heater bag must be filled with 2 litres of solution. If this time is too long for the patient to wait, it is possible to perform a partial fill of the heater bag with for example 5 dl solution produced in 4 minutes, and use this volume of fluid to prime the tubes and displace the air. Then, the patient may connect himself to the connector 208 already after 4 minutes of priming and then go to bed, while the machine produces the first fill volume. It is noted that there is normally 2 - 5 dl of solution left in the heater bag, in order to prevent complete emptying of the heater bag, because there is often some air or gas in the top of the heater bag, which should not be delivered to the patient. The first priming solution may be different from the treatment solution, for example comprising physiological sodium chloride.

It is recognized that the invention for reducing the cycle time may be used with other sources of fresh fluid, such as supply bags as is conventional in APD. In this case, a pump and possibly a flow meter is added to perform the replenishment phase during the drain phase and/or the emptying phase, when the heater bag is not used by the cycler.

Several embodiments of the invention have been described above with reference to the enclosed drawings. It will be realised that the different features may be combined in different manners than indicated and such other combinations are within the scope of the invention. The invention is only limited by the appended patent claims.

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PATENT CLAIMS

1. A method of operating a cycler intended for peritoneal dialysis, comprising a pressure chamber provided with a first bag for enclosing a fresh fluid intended to be filled to a patient and a second bag for enclosing a spent fluid intended to be drained from a patient, said first and second bag being arranged at a weighing device for weighing the combined weight thereof, **characterized** by

draining said spent fluid into said second bag supervised by the weighing device; and

replenishing said first bag at a predetermined replenishment fluid flow rate during said draining step.

2. A method as claimed in claim 1, **characterized** by exposing said first bag and said second bag for an underpressure in said pressure chamber during said draining step.

3. A method as claimed in claim 1 or 2, **characterized** by providing said replenishment fluid flow rate by a volumetric pump arranged at the inlet of said first bag.

4. A method as claimed in claim 1, 2 or 3, **characterized** by the fact that said replenishment flow rate is a constant flow rate.

5. A method as claimed in claim 4, **characterized** in that said replenishment of said first bag is performed at a constant flow rate until a predetermined replenishment volume has been introduced into said first bag.

6. A method as claimed in any of the preceding claims, **characterized** by controlling the draining step by means of said weighing device, corrected for the replenishment of said first bag by said replenishment flow rate.

7. A method as claimed in claim 6, **characterized** by interrupting said draining step when a predetermined volume has been drained into the second bag.

8. A method as claimed in claim 6, **characterized** by interrupting said draining step when a predetermined time has elapsed from the start of the draining step.

9. A method as claimed in claim 6, **characterized** by interrupting said draining step when an inlet flow rate into said second bag is below a predetermined flow rate, said inlet flow rate being determined by said weighing device.

10. A method as claimed in any of the preceding claims, **characterized** in that said inlet flow rate is determined as a change of weight of the combined first bag and second bag.

11. A method as claimed in any of the preceding claims, in which said cycler is operated in four phases, in the following order:

a drain phase for draining spent dialysate from a patient connected to said second bag;

a fill phase for filling the patient with fresh fluid from said first bag;

an emptying phase for emptying the spent dialysate in said second bag to a waste receiver;

a replenishment phase for replenishing the first bag with fresh fluid;

**characterised** by the fact that the replenishment phase and the drain phase takes place at least partially simultaneously.

12. A method as claimed in claim 11, **characterized** in that said replenishment phase is initiated during the emptying phase and in that the drain phase is initiated shortly after the termination of the emptying phase.

13. A method as claimed in claim 11 or 12, **characterized** in that:

said drain phase for draining spent dialysate from a patient connected to said second bag takes place under negative pressure in said pressure chamber;

said fill phase for filling the patient with fresh fluid from said first bag takes place under positive pressure in said pressure chamber;

said emptying phase for emptying the spent dialysate in said second bag to a waste receiver takes place under positive pressure in said pressure chamber;

said replenishment phase for replenishing the first bag with fresh fluid takes place during said emptying phase and/or said drain phase under either a positive or a negative pressure in said pressure chamber under the control of a positive displacement type pump.

14. A method as claimed in any one of claims 1 - 10, in which said cycler is operated in four phases in the following order:

a drain phase for draining spent dialysate from a patient connected to said second bag;

an emptying phase for emptying the spent dialysate in said second bag to a waste receiver;

a fill phase for filling the patient with fresh fluid from said first bag;

a replenishment phase for replenishing the first bag with fresh fluid;

**characterised** by the fact that the replenishment phase and the drain phase takes place at least partially simultaneously.

15. A method as claimed in claim 14, **characterized** in that said replenishment phase is initiated after the termination of the fill phase and continues during said drain phase and possibly also during said emptying phase.

16. A method as claimed in claim 14 or 15, **characterized** in that:

said drain phase for draining spent dialysate from a patient connected to said second bag takes place under negative pressure in said pressure chamber;

said emptying phase for emptying the spent dialysate in said second bag to a waste receiver takes place under positive pressure in said pressure chamber;

said fill phase for filling the patient with fresh fluid from said first bag takes place under positive pressure in said pressure chamber;

said replenishment phase for replenishing the first bag with fresh fluid takes place during said drain phase and/or said emptying phase under either a negative or a positive pressure in said pressure chamber under the control of a positive displacement type pump.

17. A method as claimed in any of the preceding claims, **characterized** in that during said replenishment phase, the first bag is exposed to a heating device for heating the fluid in the first bag to a temperature close to 37 degrees Celsius.

18. A method as claimed in claim 17, **characterized** in that the replenishment phase is terminated and the fill phase is initiated only when the temperature of the fluid in said first bag is close to 37 degrees Celsius.

19. A cycler intended for peritoneal dialysis, comprising a pressure chamber provided with a first bag for enclosing a fresh fluid intended to be filled to a patient and a second bag for enclosing a spent fluid intended to be drained from a patient, said first and second bag being arranged at a weighing device for weighing the combined weight thereof,

**characterized** by

a draining device for draining said spent fluid into said second bag supervised by the weighing device; and

a replenishment device for replenishing said first bag at a predetermined replenishment fluid flow rate during said draining step.

20. A cycler as claimed in claim 19, **characterized** in that said draining device is a pressure device for generating an underpressure in said pressure chamber comprising said first bag and said second bag during said draining step.

21. A cycler as claimed in claim 19 or 20, **characterized** in that said replenishment device is a volumetric pump arranged at the inlet of said first bag.

22. A cycler as claimed in claim 19, 20 or 21, **characterized** in that said volumetric pump is arranged to pump replenishment fluid into said first bag at a constant replenishment fluid flow rate.

23. A cycler as claimed in claim 22, **characterized** in that said volumetric pump is arranged to replenish said first bag at a constant replenishment fluid flow rate until a predetermined replenishment volume has been introduced into said first bag.

24. A cycler as claimed in any of claims 19 - 23, **characterized** in that said weighing device is arranged to control the draining step corrected for the replenishment of said first bag by said volumetric pump.

25. A cycler as claimed in claim 24, **characterized** in that the cycler is arranged to interrupt said draining step when a predetermined volume has been drained into the second bag.

26. A cycler as claimed in claim 24, **characterized** in that the cycler is arranged to interrupt said draining step when a predetermined time has elapsed from the start of the draining step.

27. A cycler as claimed in claim 24, **characterized** in that the cycler is arranged to interrupt said draining step when an inlet flow rate into said second bag is below a predetermined flow rate, said inlet flow rate being determined by said weighing device.

28. A cycler as claimed in any of claims 19 - 27, **characterized** in that the cycler is arranged to determine said inlet flow rate as a change of weight of the combined first bag and second bag.

29. A cycler as claimed in any of claims 19 - 28, in which said cycler is operated in four phases, in the following order:

a drain phase for draining spent dialysate from a patient connected to said second bag;

a fill phase for filling the patient with fresh fluid from said first bag;

an emptying phase for emptying the spent dialysate in said second bag to a waste receiver;

a replenishment phase for replenishing the first bag with fresh fluid;

**characterised** by the fact that the replenishment phase and the drain phase takes place at least partially simultaneously.

30. A cycler as claimed in claim 29, **characterized** in that the cycler is arranged to initiate said replenishment phase during the emptying phase and to initiate the drain phase after the termination of the emptying phase.

31. A cycler as claimed in claim 29 or 30, **characterized** in that:

said drain phase for draining spent dialysate from a patient connected to said second bag takes place under negative pressure in said pressure chamber;

said fill phase for filling the patient with fresh fluid from said first bag takes place under positive pressure in said pressure chamber;

said emptying phase for emptying the spent dialysate in said second bag to a waste receiver takes place under positive pressure in said pressure chamber;

said replenishment phase for replenishing the first bag with replenishment fluid takes place during said emptying phase and/or said drain phase under either a positive or a negative pressure in said pressure chamber under the control of a positive displacement type pump.

32. A cycler as claimed in any one of claims 19 - 28, in which said cycler is operated in four phases in the following order:

a drain phase for draining spent dialysate from a patient connected to said second bag;

an emptying phase for emptying the spent dialysate in said second bag to a waste receiver;

a fill phase for filling the patient with fresh fluid from said first bag;

a replenishment phase for replenishing the first bag with fresh fluid;

**characterised** by the fact that the replenishment phase and the drain phase takes place at least partially simultaneously.

33. A cycler as claimed in claim 32, **characterized** in that the cycler is arranged to initiate said replenishment phase after the termination of the fill phase and said replenishment phase continues during said drain phase and possibly also during said emptying phase.

34. A cycler as claimed in claim 32 or 33, **characterized** in that:

said drain phase for draining spent dialysate from a patient connected to said second bag takes place under negative pressure in said pressure chamber;

said emptying phase for emptying the spent dialysate in said second bag to a waste receiver takes place under positive pressure in said pressure chamber;

said fill phase for filling the patient with fresh fluid from said first bag takes place under positive pressure in said pressure chamber;

said replenishment phase for replenishing the first bag with fresh fluid takes place during said drain phase and/or said emptying phase under either a negative or a positive pressure in said pressure chamber under the control of a positive displacement type pump.

35. A cycler as claimed in any of claims 19 - 34, **characterized** in that a heating device is arranged to expose the first bag to heat energy, during said replenishment phase, for heating the fluid in the first bag to a temperature close to 37 degrees Celsius.

36. A cycler as claimed in claim 34, **characterized** in that the cycler is arranged to terminate the replenishment phase and

to initiate the fill phase only when the temperature of the fluid in said first bag is close to 37 degrees Celsius.

37. A cycler as claimed in any of claims 19 - 36, **characterized** in that the cycler comprises valves for controlling the fluid flow to and from the first bag and the second bag.

38. A cycler as claimed in claim 37, **characterised** by a first valve for controlling the fluid flow into said first bag from said replenishment device, a second valve for controlling the fluid flow out from said first bag to a patient line, a third valve for controlling the fluid flow into said second bag from said patient line and a fourth valve for controlling the fluid flow out from said second bag.

39. A cycler as claimed in claim 38, **characterised** in that said first valve is opened only when said second valve is closed and vice versa.

40. A cycler as claimed in claim 38 or 39, **characterised** in that said third valve is opened only when said second valve and said fourth valve is closed.

41. A cycler as claimed in claim 38 or 39, **characterised** in that said third valve is opened only when said fourth valve is closed and vice versa.

42. A cycler as claimed in claim 37, 38 or 39, **characterized** in that said pressure device is arranged to expose said pressure chamber for a positive pressure when the second valve is opened and when the fourth valve is opened, and a negative pressure when the third valve is opened, and either a positive or negative pressure when the first valve is opened.

43. A cycler as claimed in any of claims 19 - 42, **characterized** in that said first bag and said second bag are combined into an integrated double bag.

44. A cycler as claimed in any of claims 19 - 43, **characterized** in that said replenishment device comprises a pump and a flow meter for measuring the replenishment fluid flow rate.

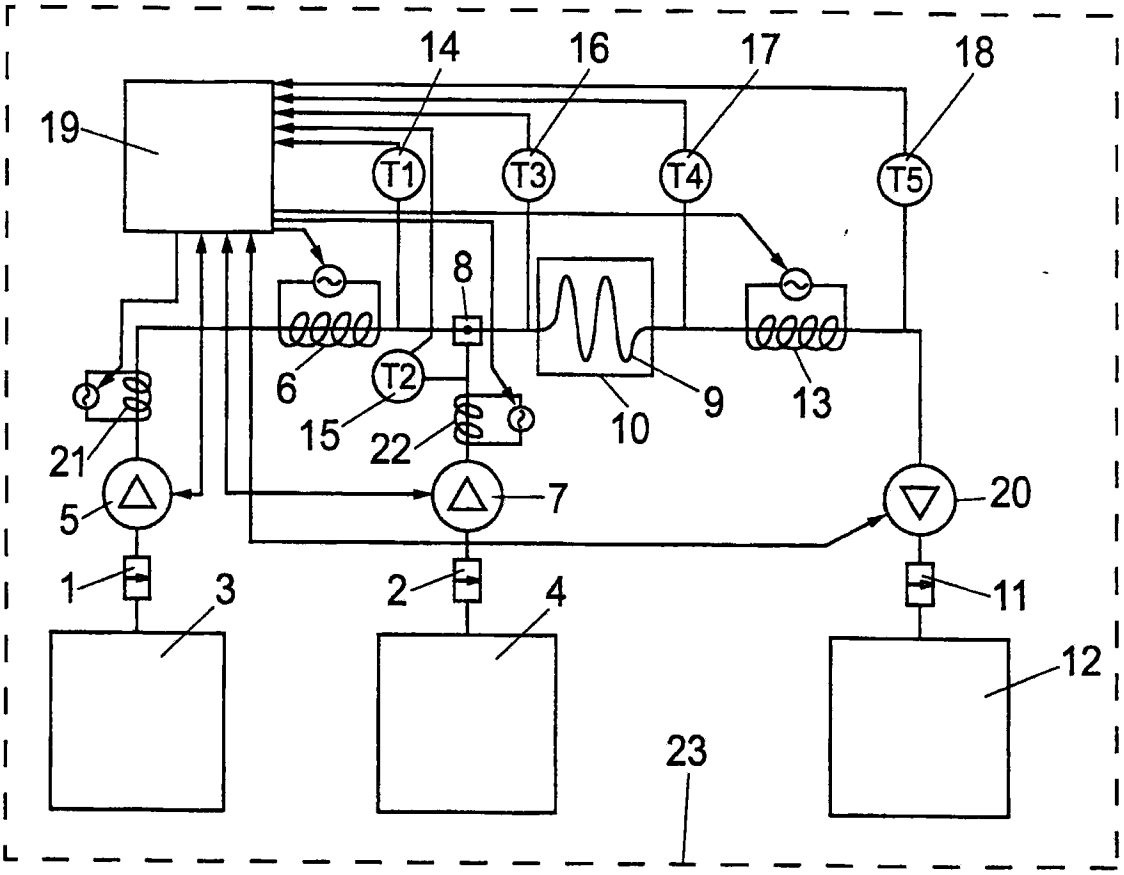


Fig. 1

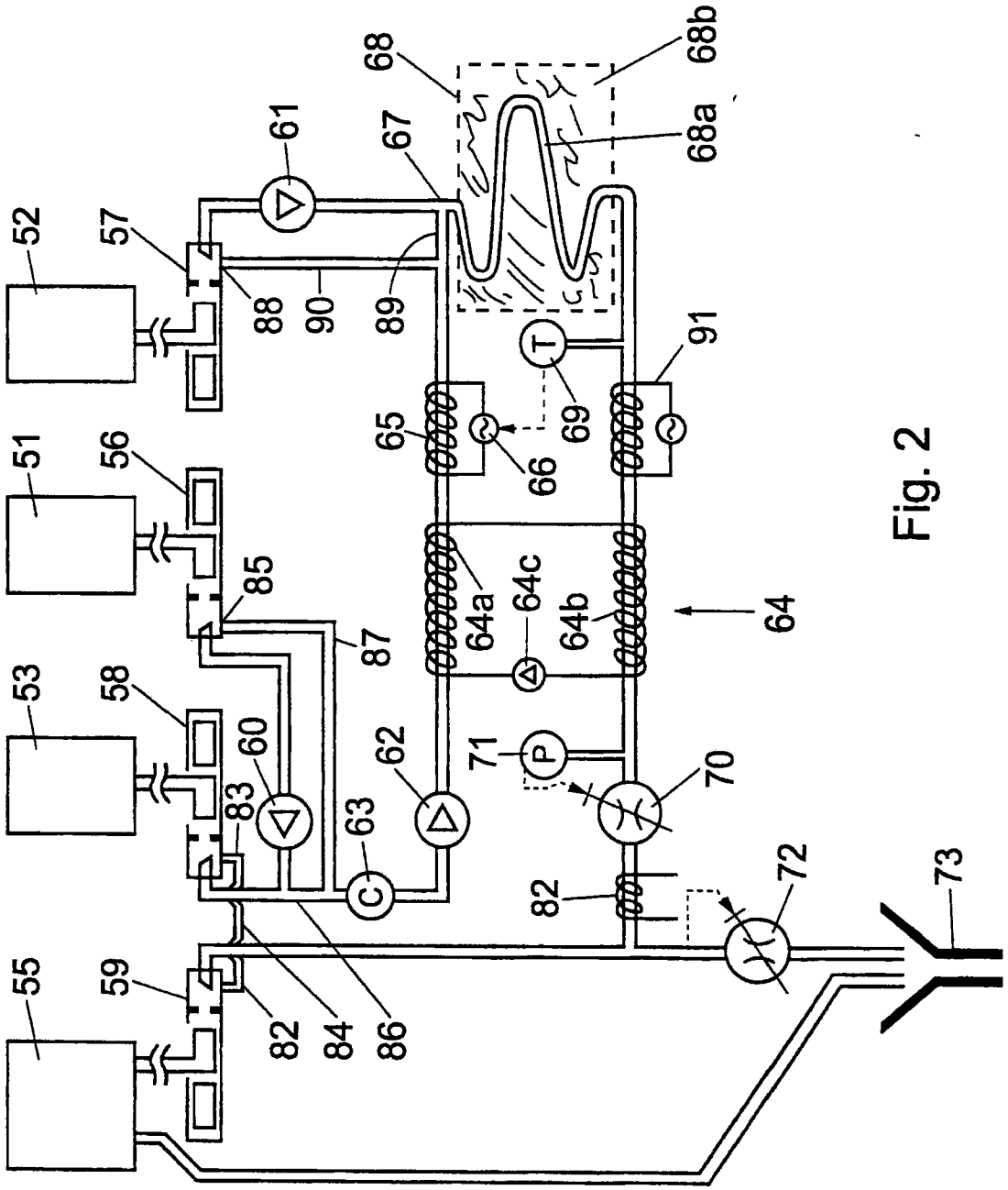
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Fig. 2

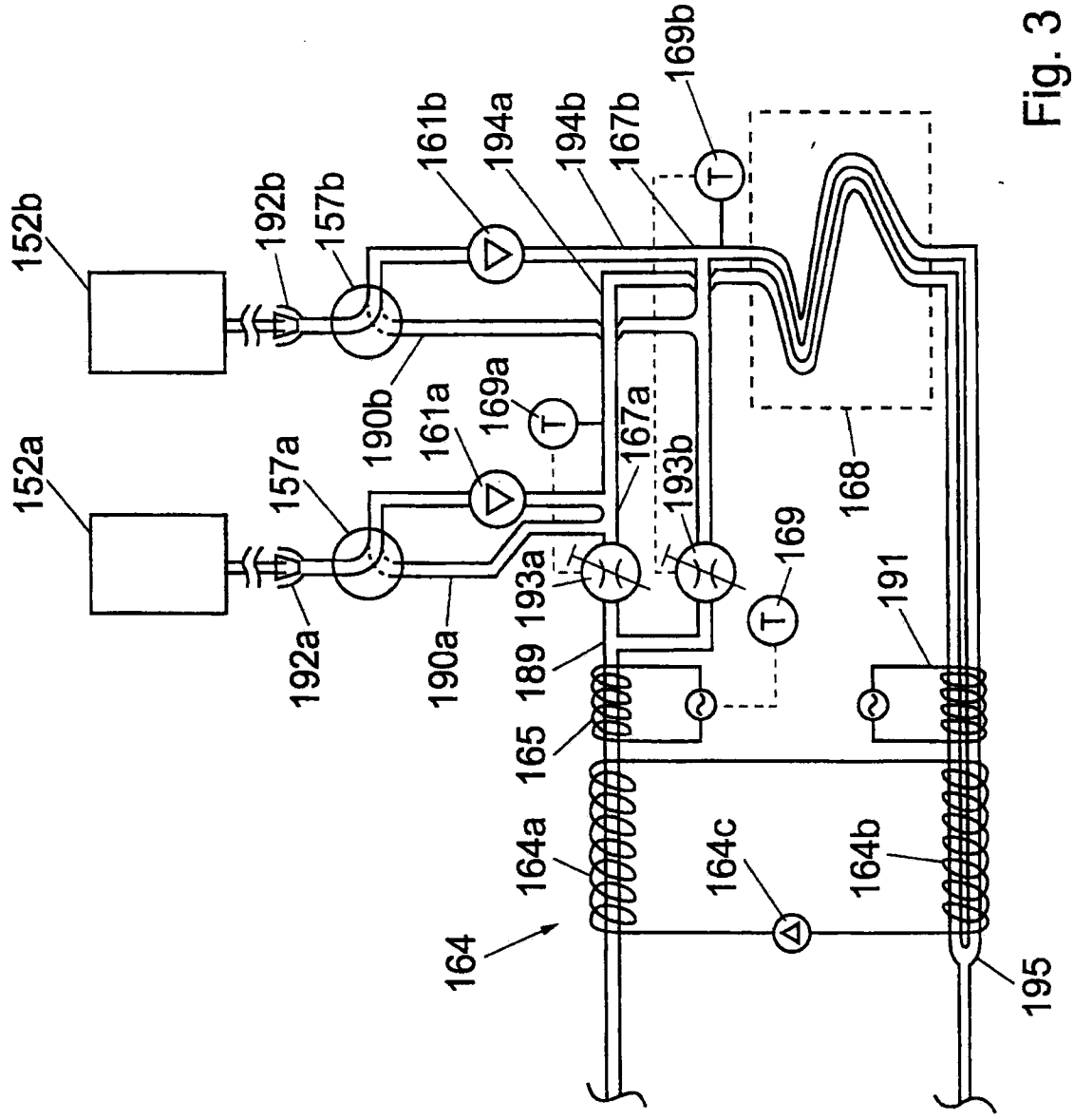
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Fig. 3

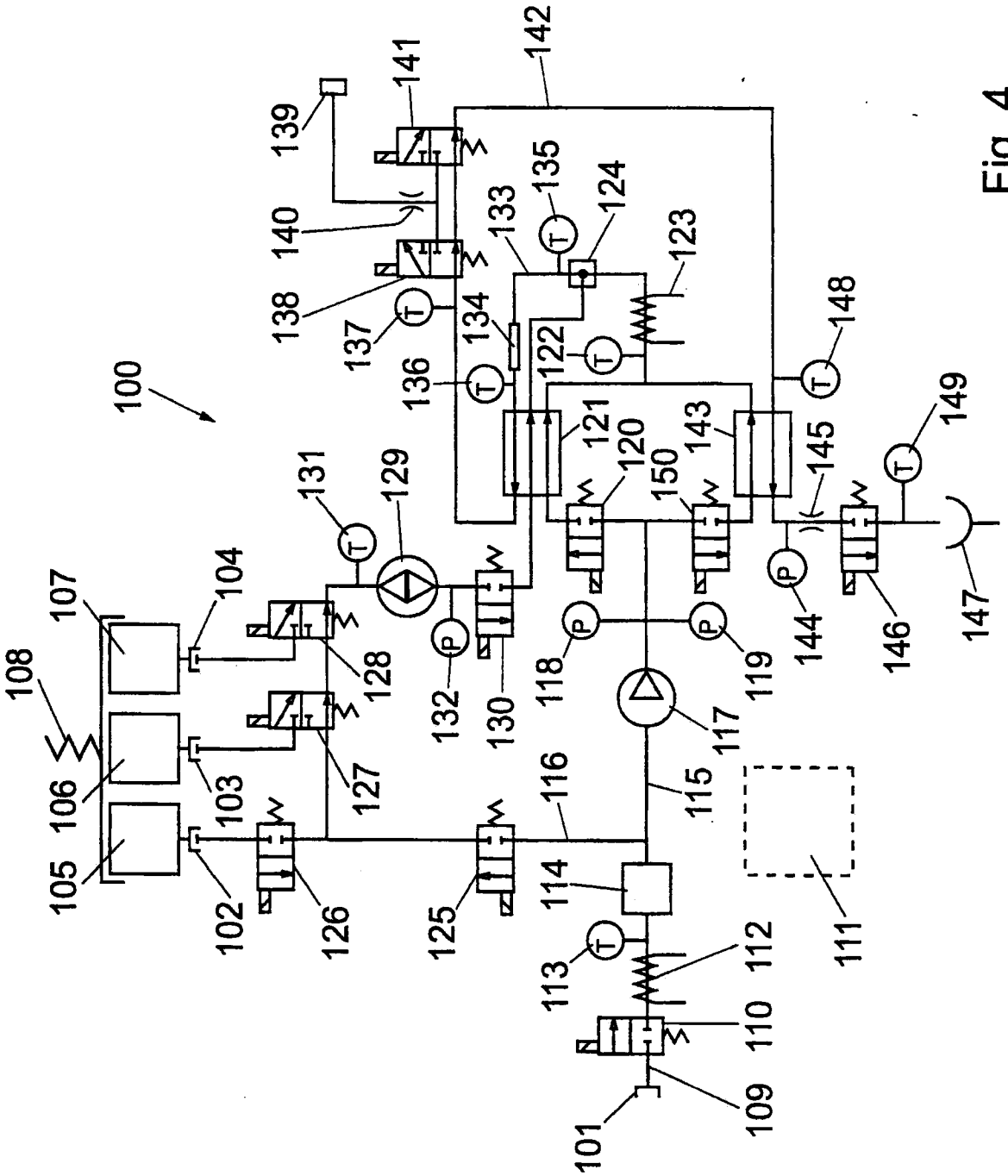
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Fig. 4

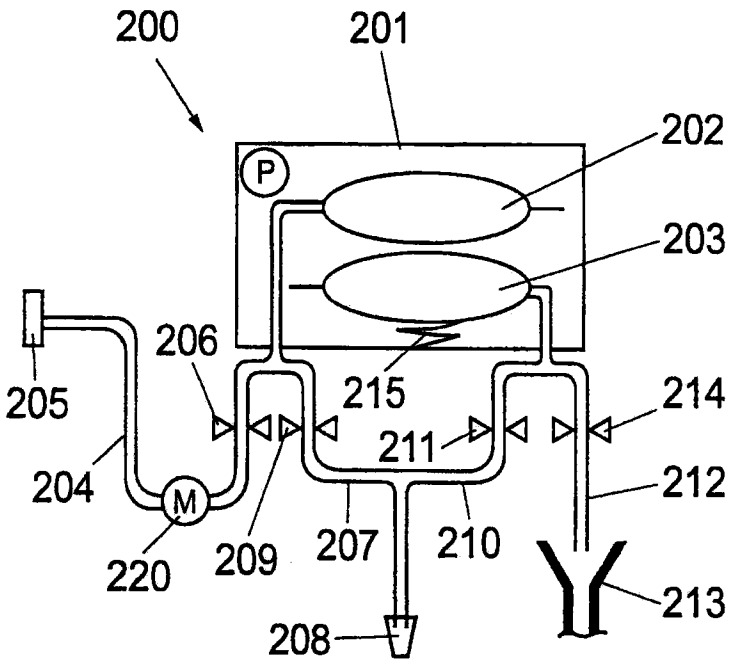
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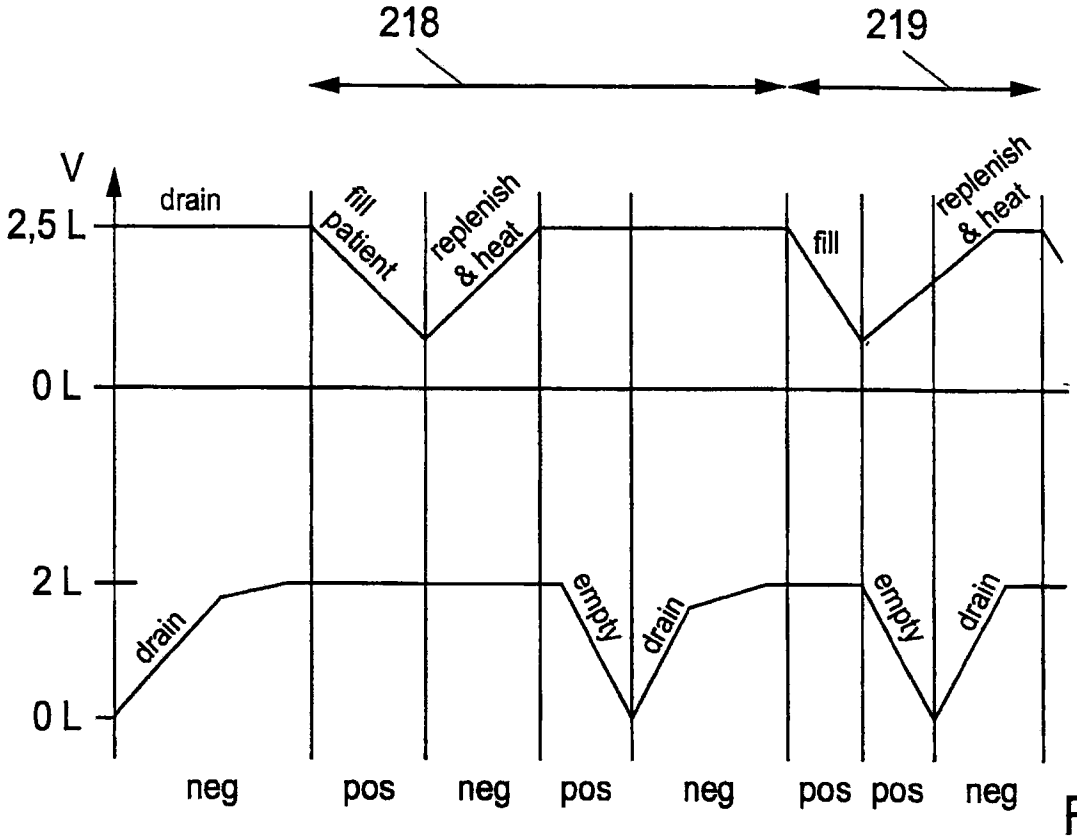
Fig. 5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replenish & heat
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Fig. 7

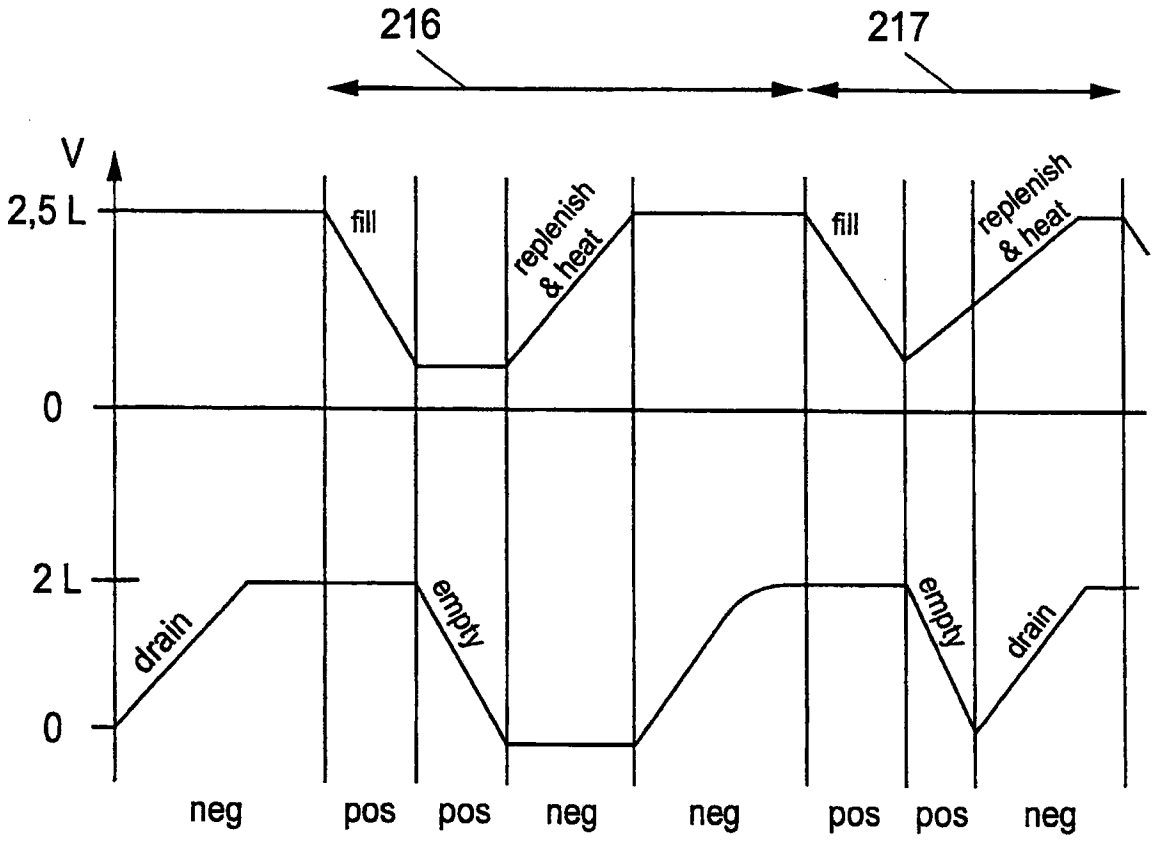
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Fig.6

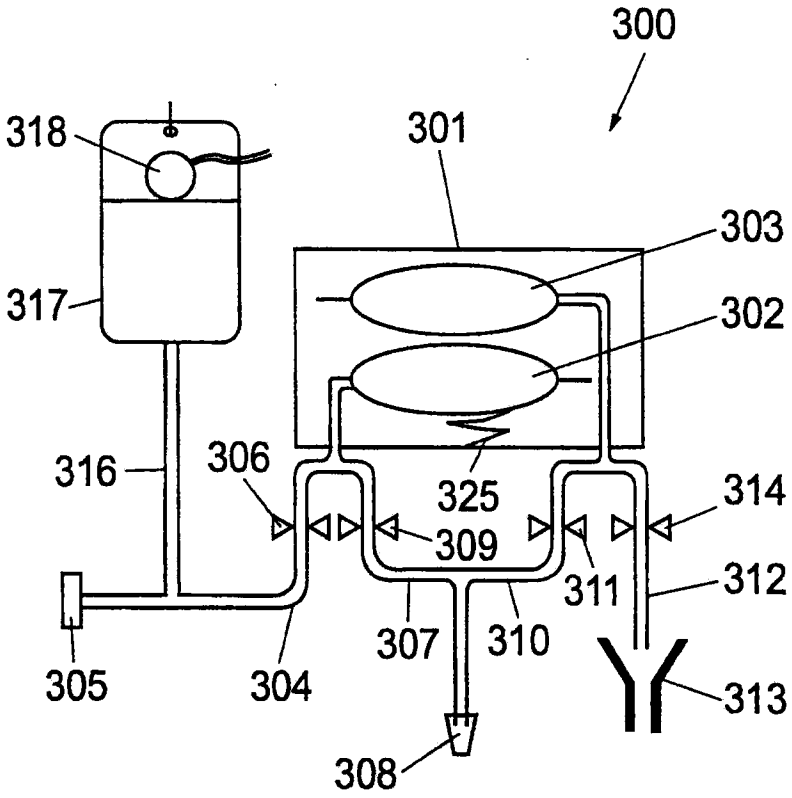
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Fig. 8

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 00/01772

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61M 1/28
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

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"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 11 December 2000 | 20 -12- 2000 |
| Name and mailing address of the ISA/ Swedish Patent Office | Authorized officer |

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 00/01772

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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04/12/00

International application No.
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